

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 7,402,660	)	Serial No. 09/918,715
	)	
Inventor(s): Brad ST. CROIX <i>et al.</i>	)	Filed: August 1, 2001
	)	
Issued Date: July 22, 2008	)	Attorney Docket No. 001107.00134

For: ENDOTHELIAL CELL EXPRESSION PATTERNS

**REQUEST FOR CERTIFICATE OF CORRECTION**

U.S. Patent and Trademark Office  
Customer Service Window  
Randolph Building, Mail Stop: Certificate of Correction Branch  
401 Dulany Street  
Alexandria, VA 22314

Sir:

Pursuant to 35 U.S.C. § 254 and 37 C.F.R. § 1.322, this is a request for the issuance of a Certificate of Correction in the above-identified patent. A copy of PTO Form 1050 is appended. The complete Certificate of Correction involves one page.

The mistakes identified in the appended Form occurred through no fault of the Applicants, as clearly disclosed by the records of the application, which matured into this patent. Enclosed for your convenience are the relevant portions of the Notice of Allowability mailed January 29, 2008, the Response to Non-Compliant Amendment filed September 25, 2006 and the initial application filed August 1, 2001.

Issuance of the Certificate of Correction containing the corrections is respectfully requested. Since these changes are necessitated through no fault of the Applicants, no fee is believed to be associated with this request. Nonetheless, should the Patent and Trademark Office determine that a fee is required, please charge our Deposit Account No. 19-0733.

Respectfully submitted,

BANNER & WITCOFF, LTD.

Dated: 09/19/2008  
Customer No. 22907

By: /Sarah A. Kagan/  
Sarah A. Kagan  
Registration No. 32,141

UNITED STATES PATENT AND TRADEMARK OFFICE  
**CERTIFICATE OF CORRECTION**

PATENT NO.: 7,402,660  
DATED: July 22, 2008  
INVENTOR(S): Brad ST. CROIX *et al*

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Column 40:

Please insert the following claims:

-- 40. The isolated molecule of claim 1 wherein said molecule binds to TEM17 at least 7 times more than to irrelevant antigen or antigen mixture.

41. The isolated molecule of claim 1 wherein said molecule binds to TEM17 at least 10 times more than to irrelevant antigen or antigen mixture.--

Prior to the Specification in Column 1:

Please insert the appended Tables 1-4.

Mailing Address of Sender:

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U.S. PAT. NO 7,402,660

No. of add'l copies  
@ \$0.50 per page

□

Table 1. Previously characterized and novel Pan Endothelial Markers (PEMs).

The most abundant tags derived by summing the tags from Normal EC (N-EC's) and Tumor EC (T-EC's) SAGE libraries are listed in descending order. N-EC and T-EC SAGE libraries contained 96,694 and 96,588 SAGE tags respectively. For comparison, the corresponding number of SAGE tags found in cultured human umbilical vein endothelial cells (HUVEC), human dermal microvascular endothelial cells (HMVEC), and non-endothelial cell lines (Cell Lines) are shown. The HUVEC SAGE library contained 290,000 tags and the HMVEC library 111,000 tags. Non-endothelial cell lines consisted of 1.8x10<sup>6</sup> tags derived from a total of 14 different cancer cell lines including colon, breast, lung, and pancreatic cancers, as well as one non-transformed keratinocyte cell line, two kidney epithelial cell lines, and normal monocytes. Tag numbers for each group were normalized to 100,000 transcripts. A 'Description' of the gene product corresponding to each tag is given, followed by alternative names in parenthesis. The sequence CATG precedes all tags and the 15th base (11th shown) was determined as previously described by Velculescu et. al. (Nat Genet 1999 Dec;23(4):387-8).

no.	Tag Sequence	N-EC's	T-EC's	HUVEC	HMVEC	Cell Lines	Description
1	CATATCATTA	247	501	130	87	2	angiomodulin (ANG, IGFBP-7, IGFBP-rP1, Mac25, TAF)
2	TGCACCTCAAG	328	141	0	0	0	hevin
3	TTTGACCTTT	165	84	191	115	4	connective tissue growth factor (CTGF, IGFBP-rP2)
4	CCCTTGCCG	131	104	1	1	0	ESTs
5	TTGCTGACCTT	73	131	2	14	1	collagen, type VI, alpha 1
6	ACCATTGGATT	102	67	0	0	2	interferon induced transmembrane protein 1 (9-27, Leu 13)
7	ACACTCTTTC	104	44	60	62	2	guanine nucleotide binding protein 11
8	TTCTGCTCTTG	71	67	118	72	0	von Willebrand factor
9	TCCCTGGCAGA	66	68	3	13	3	cysteine-rich protein 2 (CRP-2, ESP-1, SmlIM)
10	TAATCCTCAAG	26	106	34	16	1	collagen, type XVIII, alpha 1
11	ATGCTTTTCT	58	65	17	17	3	insulin-like growth factor-binding protein 4
12	GGGATTAAGC	40	67	30	14	2	CD146 (S-Endo 1, P1H12, Muc18, MCAM, Mel-CAM)
13	TTAGTGTGTA	38	69	9	13	0	SPARC (osteonectin, BM-40)
14	TTCTCCCAAAT	20	86	16	64	2	collagen, type IV, alpha 2
15	GTGCTAAGCGG	24	74	0	10	2	collagen, type VI, alpha 2
16	GTTTATGGATA	35	56	11	11	1	matrix Gla protein (MGP)
17	CCCTTTCACAC	52	33	0	0	0	ESTs, Weakly similar to HPBRII-7 protein
18	TGTTCTGGAGA	58	27	18	56	2	gap junction protein, alpha 1, 43kd (connexin 43)

19	AAGATCAAGAT	34	50	2	4	1	actin, alpha 1, skeletal muscle / actin, alpha 2, smooth muscle, aorta
20	TCTCTGAGCAT	32	48	0	0	0	aggrecanase 1 (metalloproteinase with thrombospondin type 1 motifs, 4)
21	CAGGTTTCATA	22	56	0	0	0	small inducible cytokine subfamily B (Cys-X-Cys), member 14 (BRAK)
22	GCACAAGTTCT	43	25	6	22	0	calcitonin receptor-like receptor activity modifying protein 2
23	AGCTTGTGGCC	45	23	0	0	0	calcitonin receptor-like receptor activity modifying protein 3
24	CTTCTGGATAA	13	54	12	0	0	cell division cycle 42 (GTP-binding protein, 25kD)
25	CAACAATAATA	42	25	13	6	0	ESTs
26	ACCGGCGCCCCG	50	15	0	0	0	tetranectin (plasminogen-binding protein)
27	GGAAGCTAAGT	35	27	0	5	1	osteoblast specific factor 2 (fasciclin I-like)
28	GCAATTTAACC	38	21	0	3	0	solute carrier family 21 (prostaglandin transporter), member 2
29	GATAACTACAT	18	35	4	4	0	angiomodulin (ANG, IGFBP-7, IGFBP-rP1, Mac25, TAF)
30	TATGAGGGTAA	19	30	40	2	0	regulator of G-protein signalling 5
31	CCACGGGATTC	10	39	0	0	0	collagen, type III, alpha 1
32	TTTACAAAGAG	26	21	0	1	1	carboxypeptidase E
33	CCCAGTAAGAT	22	25	0	16	1	cysteine and glycine-rich protein 2 (LIM domain only, smooth muscle)
34	ACAAAGCATT	26	20	0	14	1	Human insulin-like growth factor binding protein 5 (IGFBP5) mRNA
35	GCCTGTCCCTC	8	38	22	11	0	ESTs / biglycan
36	TACTTTATAAG	25	21	1	1	0	metalloproteinase with thrombospondin type 1 motifs (ADAMTS1, METH-1)
37	TGTTTAATACA	15	29	2	1	1	ESTs / erythrocyte membrane protein band 4.1-like 2
38	GTCCCTGCCTT	18	25	1	1	0	glutathione S-transferase M2 (muscle)
39	GAGCCATCATA	21	21	2	2	1	ESTs / GTP-binding protein

							overexpressed in skeletal muscle
40	GGCCCTACAGT	26	13	2	3	0	ESTs / KIAA0821 protein
41	GCTAACCCTCG	7	31	0	1	0	ESTs
42	ATCACACAGCT	19	18	0	0	0	thyroid and eye muscle autoantigen D1 (64kD)
43	ACAAGTACTGT	18	19	36	27	0	cadherin 5, VE-cadherin (vascular epithelium)
44	TCACCGTGGAC	20	17	0	1	0	selectin P (granule membrane protein 140kD, antigen CD62)
45	ACATTCCAAGT	18	18	0	1	1	tissue inhibitor of metalloproteinase 3
46	GAGCCTGGATA	6	29	0	0	0	chondroitin sulfate proteoglycan 4 (melanoma-associated)
47	GGCACTCCTGT	22	13	19	12	0	ESTs
48	TCACAGCCCCC	20	15	8	5	0	ESTs
49	TGCCAGGTGCA	10	23	0	1	0	albumin
50	TGGGAAACCTG	11	22	0	1	1	eukaryotic translation initiation factor 4 gamma, 1
51	TTTCATCCTACT	20	13	0	2	0	ESTs, KIAA0362 protein
52	AACAGGGGCCA	15	18	0	0	1	ESTs / interferon, alpha-inducible protein (clone IFI-6-16)
53	ACTGAAAGAAG	6	26	0	0	1	complement component 1, s subcomponent
54	ACCGTTCTGTA	8	24	10	6	0	transcription factor 4
55	ATACTATAATT	25	6	2	0	0	ESTs
56	TTTGATAGAA	17	15	4	5	1	KIAA0393 protein
57	GTAATGACAGA	20	11	1	1	1	stanniocalcin
58	AATAGGGGAAA	13	19	4	1	0	ESTs, KIAA1075 protein
59	GTGCTACTTCT	5	25	2	18	0	collagen, type IV, alpha 1
60	CCGGCCCCCTCC	6	24	0	0	1	peanut (Drosophila)-like 2
61	TTGAATTGT	19	10	1	1	0	RNA-binding protein gene with multiple splicing
62	CGAGAGTGTGA	22	6	0	0	0	ESTs
63	CCCTGTTACGC	14	15	38	24	0	tyrosine kinase with IgG and EGF homology domains (Tie)
64	CAGATGGAGGC	18	10	1	9	0	ESTs
65	AGGCTCCTGGC	8	20	0	0	0	ESTs
66	TCTGCTTCTAG	20	8	40	15	0	ESTs

67	GGCTTAGGATG	18	9	10	14	0	ESTs
68	GGTTGTTGCCG	6	21	0	0	1	ESTs
69	ACAAGTACCCA	5	22	4	5	0	P311 protein
70	CTTCTCTGAG	18	9	1	4	1	basic transcription element binding protein 1
71	GCTAATAATGT	10	17	0	2	0	KIAA1077 protein
72	TGTGCTTTTT	10	15	1	4	0	KIAA0758 protein / protein kinase, cAMP-dependent, catalytic, alpha
73	CATCACGGATC	17	8	0	1	0	interleukin 1 receptor, type 1
74	GCAGCAGCAGC	6	18	0	2	0	T-box 2
75	TGACTGTATTA	13	11	0	0	0	ESTs / amine oxidase, copper containing 3 (vascular adhesion protein 1)
76	GAATGCTCTTG	6	18	0	11	0	gap junction protein, alpha 4, 37kD (connexin 37)
77	GTAGTCTCGGA	18	6	0	5	0	ESTs, clone 23698 mRNA
78	TCCCTCTCTC	6	17	0	0	0	periodontal ligament fibroblast protein
79	GGGCAGTGGCT	5	18	12	5	0	ESTs, DKFZP586B0621 protein
80	AAATATGTGTT	19	4	13	3	0	ESTs
81	GTCATTTTCTA	11	11	10	2	0	ESTs / transcription factor 8 (represses interleukin 2 expression)
82	CTCTCCAAACC	14	8	0	0	0	complement component 1 inhibitor (angioedema, hereditary)
83	TTAATGTGTAA	4	18	0	0	0	guanylate cyclase 1, soluble, beta 3
84	TCAAGCAATCA	13	9	0	1	0	ESTs
85	GAAGACACTTG	15	7	1	0	0	ESTs
86	GGGTAGGGTGA	6	15	0	0	1	integrin, alpha 7
87	TGGAACAGTGA	10	10	10	5	0	ESTs
88	GAGTGGCTACC	10	9	0	0	0	ESTs
89	GTCAGGGTCCC	13	7	0	9	0	decidual protein induced by progesterone
90	GTCAGTCACTT	14	6	4	1	0	hairy (Drosophila)-homolog
91	AGCAGAGACAA	14	6	1	10	0	natriuretic peptide receptor A - guanylate cyclase A
92	AGCGATGGAGA	9	10	0	0	0	ESTs
93	CGTGGGGTGTA	9	10	17	3	0	

**Table 2. Previously characterized and novel Tumor Endothelial Markers (TEMs).**

The top 46 tags with the highest tumor EC (T-EC's) to normal EC (N-EC's) tag ratios are listed in descending order. To calculate tag ratios, a value of 0.5 was assigned in cases where zero tags were observed. The SAGE libraries are the same as those listed in Table 1. Tag numbers for each group were normalized to 100,000 transcripts. A 'Description' of the gene product corresponding to each tag is given, followed by alternative names in parenthesis. †; multiple tags for this gene are due to alternative polyadenylation sites.

no.	Tag Sequence	N-EC's	T-EC's	HUVEC	HMVEC	Cell Lines	Description
1	GGGGCTGCCCA	0	28	0	2	0	TEM1
2	GATCTCCGTGT	0	25	0	0	0	TEM2
3	CATTTTATCT	0	23	0	0	0	TEM3
4	CTTCTTTGAG	0	22	6	20	1	regulated in glioma-like 7-1 (Dkk-3/ REIC)
5	TATTAACCTC	0	21	1	3	1	TEM4
6	CAGGAGACCCC	0	16	2	0	0	MMP-11 (stromelysin 3)
7	GGAAATGTCAA	1	31	53	22	1	MMP-2 (gelatinase A, 72kD type IV collagenase)
8	CCTGGTTCAGT	0	15	0	0	0	ESTs
9	TTTTTAAGAAC	0	14	1	4	0	TEM5
10	TTTGGTTTCC	5	139	0	16	0	collagen, type I, alpha 2, transcript A†
11	ATTTGTATGA	0	13	4	8	0	nidogen (entactin)
12	ACTTTAGATGG	1	23	0	15	0	collagen, type VI, alpha 3
13	GAGTGAGACCC	3	63	0	0	1	Thy-1 cell surface antigen
14	GTACACACACC	0	10	0	0	0	ESTs / cystatin S
15	CCACAGGGGAT	2	38	0	2	1	collagen, type III, alpha 1
16	TTAAAAGTCAC	1	19	1	3	1	TEM6
17	ACAGACTGTTA	4	74	0	0	0	TEM7
18	CCACTGCAACC	1	18	0	1	0	
19	CTATAGGAGAC	1	18	1	1	0	TEM8
20	GTTCCACAGAA	0	9	0	3	0	collagen, type I, alpha 2, transcript B†
21	TACCACCTCCC	0	9	4	1	1	ESTs / pregnancy specific beta-1 glycoprotein 1
22	GCCCTTCTCT	1	17	3	1	2	TEM9 (endo180 lectin)
23	TTAAATAGCAC	2	33	0	4	0	collagen, type I, alpha 1
24	AGACATACTGA	1	16	1	0	0	ESTs, DKFZP434G162 protein
25	TCCCCCAGGAG	1	16	0	0	0	bone morphogenetic protein 1 (metalloprotease)

26	AGCCCAAAGTG	0	8	0	0	0	
27	ACTACCATAAC	0	8	0	0	0	slit (Drosophila) homolog 3 (MEGF5)
28	TACAAATCGTT	0	8	0	0	0	KIAA0672 gene product
29	TTGGGTGAAAA	0	8	0	0	0	ESTs
30	CATTATCCAAA	0	8	0	0	0	integrin, alpha 1
31	AGAAACCACGG	0	8	2	7	0	collagen, type IV, alpha 1
32	ACCAAAACCAC	0	8	0	3	0	
33	TGAAATAAAC	0	8	3	1	1	
34	TTTGGTTTCC	1	15	0	0	0	ESTs
35	GTGGAGACGGA	1	15	1	2	1	ESTs
36	TTTGTGTTGTA	1	14	2	0	0	collagen, typeXII, alpha 1
37	TTATGTTTAAT	3	39	0	0	1	lumican
38	TGGAATGACC	15	179	0	40	0	ESTs / collagen, type I, alpha 1
39	TGCCACACAGT	1	13	0	2	0	transforming growth factor, beta 3
40	GATGAGGAGAC	3	35	0	18	1	collagen, type I, alpha 2, transcript C1
41	ATCAAAGGTTT	2	23	0	0	0	ESTs, DKFZp564O222 mRNA
42	AGTCACATAGT	1	11	2	0	0	ESTs / cell division cycle 42 (GTP-binding protein)
43	TTCGGTGGTC	4	45	0	19	0	
44	CCCCACAGGG	2	21	0	0	0	ESTs
45	GGCTTGCCTTT	1	10	0	10	1	
46	ATCCCTTCCCG	1	10	1	0	0	peanut-like protein 1



**Table 3. Previously characterized and novel Normal Endothelial Markers (NEMs).**

The top 33 tags with the highest normal EC (N-EC's) to tumor EC (T-EC's) tag ratios are listed in descending order. To calculate tag ratios, a value of 0.5 was assigned in cases where zero tags were observed. The SAGE libraries are the same as those listed in Table 1. Tag numbers for each group were normalized to 100,000 transcripts. A 'Description' of the gene product corresponding to each tag is given, followed by alternative names in parenthesis.

no.	Tag Sequence	N-EC's	T-EC's	HUVEC	HMVEC	Cell Lines	Description
1	TCTCACGTCTC	26	0	0	0	0	mucosal vascular addressin cell adhesion molecule 1
2	CTAGCGTTTTA	19	0	4	14	0	serum deprivation response (phosphatidylserine-binding protein)
3	GTGGCTGACGC	18	0	1	0	0	ESTs / intercellular adhesion molecule 4
4	CTCTTAAAAA	34	1	1	0	0	small inducible cytokine subfamily A (Cys-Cys), member 14
5	TGCGAAGAGGG	16	0	3	4	1	ESTs
6	GTTTAAGGATG	16	0	0	0	0	ESTs
7	CTTTGTTTTGC	15	0	56	32	1	endothelin 1
8	ATTGCCAATCT	14	0	0	4	0	TU3A protein
9	TGTTGAAAAA	21	1	1	0	0	E-selectin (endothelial adhesion molecule 1)
10	ACAAAAAGGCC	21	1	0	6	0	TU3A protein
11	AAGATGCACAC	21	1	1	1	1	phosphodiesterase 1 - nucleotide pyrophosphatase 2 (autotaxin)
12	GTAGAGGAAAA	10	0	0	9	0	
13	TTGTTCAAGGG	10	0	0	1	0	ESTs
14	CTCTTCAAAAA	19	1	1	0	0	small inducible cytokine subfamily A, member 14
15	TATTAATAG	18	1	6	9	1	transforming growth factor, beta receptor II (70-80kD)
16	GAATTCACCAG	9	0	1	14	0	ESTs
17	AAGGAGAACTG	9	0	0	0	0	small inducible cytokine subfamily A, member 14
18	AATATCTGACT	9	0	2	2	2	active BCR-related gene
19	TCAGTGACCAG	17	1	4	7	2	protein kinase C eta
20	GCAAAGTGCCC	32	2	1	5	0	ESTs
21	TAAATACTTGT	8	0	2	0	0	ESTs

22	GTCACAAATT	8	0	1	0	0	ESTs
23	ATAACCTGCAG	8	0	0	0	0	signaling lymphocytic activation molecule
24	TGCATCTGTGC	46	3	1	1	0	ESTs / glycogenin 2
25	TAAAGGCACAG	15	1	4	3	0	LIM binding domain 2
26	GACCGCGGCTT	73	5	11	7	0	claudin 5
27	ACTCCGGTGTG	14	1	0	8	0	ESTs
28	CTTCTCACCTA	27	2	3	1	0	GTP-binding protein
29	TCGTGCTTTGT	13	1	0	0	0	ESTs
30	GAGCAGTGCTG	13	1	4	2	1	feline sarcoma viral (v-fes) - Fujinami avian sarcoma viral (v-fps) homolog
31	CTCTAAAAAAA	10	1	0	1	0	ESTs
32	GAAACCCGGTA	10	1	0	0	1	phospholipase C, beta 4
33	AACACAGTGCC	10	1	7	15	1	ESTs

**Table 4. Detection of transcripts in various tumor types by RT-PCR and in situ hybridization (ISH).**

The "+" sign indicates the presence of a robust RT-PCR product or strong positive staining of vessels by in situ hybridization. The "-" sign indicates an undetectable signal by in situ hybridization or an absent or barely detectable transcript by RT-PCR. The "+/-" sign indicates a very weak signal in a limited number of vessels by in situ hybridization. "ND" indicates not determined.

		TEM1	TEM3	TEM4	TEM5	TEM7	TEM8	TEM9	vWF	Hevin
<b>RT-PCR</b>	ColonNor.	-	-	-	-	-	-	-	+	ND
	Colon Tum.	+	+	+	+	+	+	+	+	ND
<b>ISH</b>	ColonNor.	-	-	-	-	-	-	-	+	+
	Colon Tum.	+	+	+	+	+	+	+	+	+
	Liver Met.	+	+/-	+	+	+	+	+	+/-	ND
	Lung Tum.	+	ND	+	+	+	+	+	+	+
	Brain Tum.	+	ND	ND	ND	+	ND	ND	+	+
	Corpus Lut.	+	+	+	+	+	-	+	+	+
	Wound	+	ND	+	ND	+/-	+/-	ND	+	+

\* hevin was localized to both endothelial cells and malignant cells in brain tissue.



## UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,715	08/01/2001	Brad St. Croix	001107.00134	2480

22907 7590 01/29/2008  
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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT

PAPER NUMBER

1643

MAIL DATE

DELIVERY MODE

01/29/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

# **Notice of Allowability**

Application No.

09/918,715

Examiner

Christopher H. Yaen

Applicant(s)

ST. CROIX ET AL.

Art Unit

1643

**- The MAILING DATE of this communication appears on the cover sheet with the correspondence address-**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 7/30/2007.
2. ☒ The allowed claim(s) is/are 1-10 and 18-41.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All b) ☐ Some\* c) ☐ None of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
  5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
    - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
    - (b) ☐ Including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

## **Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08),  
Paper No./Mail Date \_\_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

/Christopher Yaen/  
Primary Examiner  
Art Unit 1643

**SUPPLEMENTAL EXAMINER'S AMENDMENT**

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

The application has been amended as follows:

Claims 1-10 and 18-41 are allowed.

\*\*\* Please note that the notice of allowance mailed 11/2/2007 indicated claims 1-10 and 18-39 as being allowable. However, because of scanning errors, those pages including claims 40-41 were not rescanned into the system. Claims 40 and 41 were added before final action (see amendment mailed 9/13/2006).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



TIN

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application Of:	)	Group Art Unit: 1643
ST. CROIX et al.	)	Examiner: C. Yaen
Serial No.: 09/918,715	)	Confirmation No. 2480
Filed: August 1, 2001	)	Docket No. 001107.00134
For: <b>ENDOTHELIAL CELL EXPRESSION</b>	)	
<b>PATTERNS</b>	)	

**RESPONSE**

Commissioner for Patents  
Post Office Box 1450  
Alexandria, Virginia 22313-1450

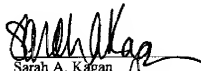
Dear Sir:

In response to the Notice of Non-Compliant Amendment mailed September 18, 2006,  
applicants resubmit the attached list of claims with a complete listing of all of the claims.

Respectfully submitted,

Dated: September 25, 2006

By:

  
Sarah A. Kagan  
Registration No. 33,141

Banner & Witcoff, Ltd.  
Customer No. 22907

40. (New) The isolated molecule of claim 1 wherein said molecule binds to TEM17 at least 7 times more than to irrelevant antigen or antigen mixture.

41. (New) The isolated molecule of claim 1 wherein said molecule binds to TEM17 at least 10 times more than to irrelevant antigen or antigen mixture.



Please type a plus sign (+) inside this box ☐

PTO/5B/05 (11-00)

Approved for release through 10/31/2002. OMB 0651-0032

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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UTILITY  
PATENT APPLICATION  
TRANSMITTAL

Attorney Docket No.	01107.00134
First Inventor	Brad St. Croix
Title	ENDOTHELIAL CELL EXPRESSION PATTERNS
Express Mail Label No.	

(Only for new nonprovisional applications under 37 C.F.R. 1.53(b))

## APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

1. ☐ Fee Transmittal Form (e.g., PTO/5B/17)  
(Submit an original and a duplicate for fee processing)
2. ☐ Applicant claims small entity status.  
See 37 CFR 1.27.
3. ☒ Specification [Total Pages 305]  
(preferred arrangement set forth below)  
- Descriptive title of the invention  
- Cross References to Related Applications  
- Statement Regarding Fed sponsored R & D  
- Reference to sequence listing, a table, or a computer program listing appendix  
- Background of the invention  
- Brief Summary of the invention  
- Brief Description of the Drawings (if filed)  
- Detailed Description  
- Claim(s)  
- Abstract of the Disclosure
4. ☒ Drawing(s) (35 U.S.C. 113) [Total Sheets 4]  
a. ☐ Newly executed (original or copy)  
b. ☐ Copy from a prior application (37 CFR 1.63 (d))  
(for a continuation/divisional with Box 18 completed)  
c. ☐ DELETION OF INVENTOR(S)  
Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b).
6. ☐ Application Data Sheet. See 37 CFR 1.76

## ADDRESS TO:

Assistant Commissioner for Patents  
Box Patent Application  
Washington, DC 20231

7. ☐ CD-ROM or CD-R in duplicate, large table or Computer Program (Appendix)
8. Nucleotide and/or Amino Acid Sequence Submission (if applicable, all necessary)  
a. ☒ Computer Readable Form (CRF)  
b. Specification Sequence Listing on:  
i. ☐ CD-ROM or CD-R (2 copies); or  
ii. ☒ paper  
c. ☐ Statements verifying identity of above copies

## ACCOMPANYING APPLICATIONS PARTS

9. ☐ Assignment Papers (cover sheet & document(s))
10. ☐ 37 C.F.R. §3.73(b) Statement of Power of Attorney (when there is an assignee)
11. ☐ English Translation Document (if applicable)
12. ☐ Information Disclosure Statement (IDS)/PTO-1449 ☐ Copies of IDS Citations
13. ☐ Preliminary Amendment
14. ☒ Return Receipt Postcard (MPEP 503) (Should be specifically itemized)
15. ☐ Certified Copy of Priority Document(s) (if foreign priority is claimed)
16. ☐ Request and Certification under 35 U.S.C. 122 (b)(2)(B)(i). Applicant must attach form PTO/5B/35 or its equivalent.
17. ☐ Other: Tables 1-4 (8 pages). The content of the paper and computer readable forms are believed to be identical.

18. If a CONTINUING APPLICATION, check appropriate box, and supply the requisite information below and in a preliminary amendment, or in an Application Data Sheet under 37 CFR 1.76:

☐ Continuation ☐ Divisional ☐ Continuation-in-part (CIP) of prior application No. \_\_\_\_\_ / \_\_\_\_\_  
Prior application information: Examiner \_\_\_\_\_ Group / Art Unit: \_\_\_\_\_

For CONTINUATION or DIVISIONAL APPS only: The entire disclosure of the prior application, from which an oath or declaration is supplied under Box 5b, is considered a part of the disclosure of the accompanying or divisional application and is hereby incorporated by reference. The incorporation can only be relied upon when a portion has been inadvertently omitted from the submitted application parts.

## 17. CORRESPONDENCE ADDRESS

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Name (Print/Type)

SARAH A. KAGAN

Registration No. (Attorney/Agent)

32,141

Signature

Sarah A. Kagan

Date

August 2, 2001

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Box Patent Application, Washington, DC 20231

PEM's  
complete with table # 25 (PEM3) + 47 (PEM6) are G1, rest are G3

Table 1. Previously characterized and novel Pan Endothelial Markers. The most abundant tags derived by summing the tags from Normal EC (N-ECs) and Tumor EC (T-ECs) SAGE libraries are listed in descending order. N-EC and T-EC SAGE libraries contained 99,694 and 95,568 SAGE tags respectively. For comparison, the corresponding number of SAGE tags found in cultured human umbilical vein endothelial cells (HUVEC), human dermal microvascular endothelial cells (HMEC), and non-endothelial cell lines (Cell Lines) are shown. The HUVEC SAGE library contained 290,000 tags and the HMEC library 111,000 tags. Non-endothelial cell lines consisted of 1.8x10<sup>5</sup> tags derived from a total of 14 different cancer cell lines including colon, breast, lung, and pancreatic cancers, as well as one non-transformed keratinocyte cell line, two kidney epithelial cell lines, and normal monocytes. Tag numbers for each group were normalized to 100,000 transcripts. A description of the gene product corresponding to each tag is given, followed by alternative names in parentheses. The sequence CATG precedes all tags and the 15th base (11th shown) was determined as previously described by Velculescu et al. (Nat Genet 1999 Dec23(4):387-9).

no.	Tag Sequence	N-ECs	T-ECs	HUVEC	HMEC	Cell Lines	Description
1	CATATCATTA	247	501	130	87	2	angiomodulin (ANG), IGFBP-7, IGFBP-rP1, Mac25, TAF
2	TGCATCTCAAG	328	141	0	0	0	hevin
3	TTTGCACCTTT	165	84	191	115	4	connective tissue growth factor (CTGF), IGFBP-rP2
4	CCCTTGTCGG	131	104	1	1	0	ESTs
5	TTGCTGACTTT	73	131	2	14	1	collagen, type VI, alpha 1
6	ACCATTTGGATT	102	67	0	0	2	Interferon induced transmembrane protein 1 (9-27, Lau 13)
7	ACACTTCTTC	104	44	60	62	2	guanine nucleotide binding protein 11
8	TTCTGCTCTTG	71	67	118	72	0	von Willebrand factor
9	TCCTGTGCGAG	66	68	3	13	3	cysteine-rich protein 2 (CRP-2, ESP-1, Smlm)
10	TAATCTCAAG	26	103	34	18	1	collagen, type XVIII, alpha 1
11	ATGCTTTTCT	58	65	17	17	3	Insulin-like growth factor-binding protein 4
12	GGATTAAGC	40	67	30	14	2	CD148 (S-Endo 1, P1H12, Muc16, MCAM, Mol-CAM)
13	TTAGTTCGTA	38	69	9	13	0	SPARC (osteonectin, BM-40)
14	TTCTCCCAAT	20	86	16	64	2	collagen, type IV, alpha 2
15	GTGCTAAGCGG	24	74	0	10	2	collagen, type VI, alpha 2
16	GTATTGAGTA	35	58	11	11	1	matrix GII protein (MGP)
17	CCCTTTACAC	52	33	0	0	0	ESTs, Weakly similar to HPBRII-7 protein
18	TTCTCTGGAGA	58	27	13	56	2	gap junction protein, alpha 1, 43kD (connexin 43)
19	AAGATCAAGAT	34	50	2	4	1	actin, alpha 1, skeletal muscle / actin, alpha 2, smooth muscle, aorta
20	TCTGTGACAT	32	48	0	0	0	aggrucanase 1 (metalloproteinase with thrombospondin type 1 motifs, 4)
21	CAGGTTTCAT	22	56	0	0	0	small inducible cytokines subfamily B (Cys-X-Cys), member 14 (BRAC)
22	GCACAAAGTTCT	43	25	6	22	0	calcitonin receptor-like receptor activity modifying protein 2
23	ACCTTGTGGCC	45	23	0	0	0	calcitonin receptor-like receptor activity modifying protein 3
24	CTTCTGGATA	13	54	12	0	0	cell division cycle 42 (GTP-binding protein, 25kD)
25	GAGCAATAATA	42	25	13	6	0	ESTs



64	CAGATGAGGC	18	10	1	9	0	ESTs
65	AGGTCCTGGC	8	20	0	0	0	ESTs
66	TCTGCTTCTAG	20	9	40	15	0	ESTs
67	GGCTTAGGATG	18	9	10	14	0	ESTs
68	GGTTGTTCGG	6	21	0	0	1	ESTs
69	ACAAGTACCCA	5	22	4	5	0	PS11 protein
70	CTTCTCTTGAG	18	9	1	4	1	basic transcription element binding protein 1
71	GCTAATAATGT	10	17	0	2	0	KIAA1077 protein
72	TGTGCTTTTT	10	15	1	4	0	KIAA0756 protein / protein kinase, cAMP-dependent, catalytic, alpha
73	CATCAGGATC	17	8	0	1	0	interleukin 1 receptor, type 1
74	GCAGCAGCAGC	6	18	0	2	0	T-box 2
75	TGACTGTATTA	13	11	0	0	0	ESTs / aniline oxidase, copper containing 3 (vascular adhesion protein 1)
76	GAATGCTCTG	6	18	0	11	0	gap junction protein, alpha 4, 37kD (connexin 37)
77	GTAGTCTGGA	18	6	0	5	0	ESTs, clone 23688 mRNA
78	TCCCTCTCTC	6	17	0	0	0	periodontal ligament fibroblast protein
79	GGCAGTGGCT	5	18	12	5	0	ESTs, DKFZF566B0621 protein
80	AAATATGTIT	19	4	13	3	0	ESTs
81	GTCAATTTCTA	11	11	10	2	0	transcription factor 8 (represses interleukin 2 expression)
82	CTCTCCAAAGC	14	8	0	0	0	complement component 1 inhibitor (angiodenine, hereditary)
83	TTAATGTGTA	4	18	0	0	0	guanylate cyclase 1, soluble, beta 3
84	TCAAGCAATGA	13	9	0	1	0	ESTs
85	GAAGACACTTG	15	7	1	0	0	Integrin, alpha 7
86	GGGTAGGGTGA	6	15	0	0	1	ESTs
87	TGGAAACAGTA	10	10	10	5	0	ESTs
88	GAGTGGGTACG	10	9	0	0	0	decidual protein induced by progesterone
89	GTACAGGTCGC	13	7	0	9	0	halcy (Drosophila)-homolog
90	GTACGTCACTT	14	8	4	1	0	natriuretic peptide receptor A - guanylate cyclase A
91	AGCAGAGACAA	14	6	1	10	0	ESTs
92	AGCATGGAGA	9	10	0	0	0	ESTs
93	CGTGGGTGTA	9	10	17	3	0	ESTs

TEMs complete web table

Table 2. SAGE tags elevated in tumor endothelium. The top 46 tags with the highest tumor EC (T-ECs) to normal EC (N-ECs) tag ratios are listed in descending order. To calculate tag ratios, a value of 0.5 was assigned in cases where zero tags were observed. The SAGE libraries are the same as those listed in Table 1. Tag numbers for each group were normalized to 100,000 transcripts. A 'Description' of the gene product corresponding to each tag is given, followed by alternative names in parentheses. †, multiple tags for this gene are due to alternative polyadenylation sites.

no.	Tag Sequence	N-EC's	T-EC's	HUVEC	HMVEC	Cell Lines	Description
1	GGGCTGCCCA	0	28	0	2	0	ESTs, similarity to thrombospondin
2	GATCTCCGTGT	0	25	0	0	0	ESTs, similarity to rat Rhesus ras-related protein
3	CATTTTATGT	0	23	0	0	0	ESTs
4	CTTTCTTTGAG	0	22	6	20	1	regulated in glioma-like 7-1 (Dkk-3) (REIC)
5	TATTAAGTCTC	0	21	1	3	1	ESTs, similarity to JNK interacting protein-3a
6	CAGGAGACCC	0	16	2	0	0	MMP-11 (stromelysin 3)
7	GGAAATGTCAA	1	31	53	22	1	MMP-2 (gelatinase A, 72kD type IV collagenase)
8	CCTGGTTCAGT	0	15	0	0	0	ESTs
9	TTTTAAGAAC	0	14	1	4	0	ESTs
10	TTTGTTTTCC	5	139	0	16	0	collagen, type I, alpha 2, transcript A'
11	ATTTTGTATGA	0	13	4	8	0	collagen, type I, alpha 2, transcript A'
12	ACTTTAGATGG	1	23	0	15	0	collagen, type VI, alpha 3
13	GAGTGAGACCC	3	63	0	0	1	Thy-1 cell surface antigen
14	GTACACACCC	0	10	0	0	0	ESTs / cytalin 5
15	CCACAGGGGAT	2	38	0	2	1	collagen, type III, alpha 1
16	TTAAAGTCAAC	1	18	1	3	1	ESTs
17	ACAGAGTGTTA	4	74	0	0	0	ESTs, similarity with sea squirt nidogen
18	CCAGTGCAACC	1	18	0	1	0	ESTs
19	CTATAGAGAC	1	18	1	1	0	ESTs, similarity with homeobox protein DLX-3
20	GTTCACAGAAA	0	9	0	3	0	collagen, type I, alpha 2, transcript B'
21	TACCACCTCCG	0	9	4	1	1	ESTs / pregnancy specific beta-1-glycoprotein 1
22	GCCCTTTCTCT	1	17	3	1	2	endo180 lectin
23	TTAAATAGCAC	2	33	0	4	0	collagen, type I, alpha 1
24	AGACATACTGA	1	18	1	0	0	ESTs, DKFZP434G162 protein
25	TCCCCACAGGAG	1	16	0	0	0	bona morphogenetic protein 1 (metalloproteinase)
26	AGCCCAAGTGT	0	8	0	0	0	sit (Drosophila) homolog 3 (MEGF5)
27	ACTACCCATAAC	0	8	0	0	0	KIAA0672 gene product
28	TACAAATCGTGT	0	8	0	0	0	

28	TTGGTGAAAA	0	8	0	0	0	0	ESTs
30	CATTATCCAAA	0	8	0	0	0	0	integrin, alpha 1
31	AGAAACCCACGG	0	8	2	7	0	0	collagen, type IV, alpha 1
32	ACCAAACCCAC	0	8	0	3	0	0	
33	TGAAATAAAC	0	8	3	1	1	1	ESTs
34	TTTGGTTTCC	1	15	0	0	0	0	ESTs
35	GTGGAGACGGA	1	15	1	2	1	1	ESTs
36	TTTGTGTGTA	1	14	2	0	0	0	collagen, typeXII, alpha 1
37	TTATGTTTAT	3	39	0	0	1	1	lunatic
38	TGGAATGACC	15	179	0	40	0	0	ESTs / collagen, type I, alpha 1
39	TGCCACACAGT	1	13	0	2	0	0	transforming growth factor, beta 3
40	GATGAGGAGAC	3	35	0	18	1	1	collagen, type I, alpha 2, transcript C1
41	ATCAAAGGTTT	2	23	0	0	0	0	ESTs, DKFZp584O222 mRNA
42	AGTCACATAGT	1	11	2	0	0	0	cell division cycle 42 (GTP-binding protein)
43	TTGGTITGGTC	4	45	0	19	0	0	
44	CCCCACACGGG	2	21	0	0	0	0	ESTs
45	GGCTTGCCTTT	1	10	0	10	1	1	
46	ATCCCTTCCCG	1	10	1	0	0	0	peanut-like protein 1

Table 3. Detection of transcripts in various tumor types by RT-PCR and in situ hybridization (ISH). The "+," sign indicates the presence of a robust RT-PCR product or strong positive staining of vessels by in situ hybridization. The "-" sign indicates an undetectable signal by in situ hybridization or an absent or barely detectable transcript by RT-PCR. The "+/-" sign indicates a very weak signal in a limited number of vessels by in situ hybridization.

	TEM1	TEM3	TEM4	TEM5	TEM7	TEM8	TEM9	vWF	Hevin
RT-PCR									
Colon Nor.	-	-	-	-	-	-	-	+	ND
Colon Tum.	+	+	+	+	+	+	+	+	ND
Colon Nor.	-	-	-	-	-	-	-	+	+
Colon Tum.	+	+	+	+	+	+	+	+	+
Liver Met.	+	+/-	+	+	+	+	+	+/-	ND
Lung Tum.	+	ND	+	+	+	+	+	+	+
Brain Tum.	+	ND	ND	ND	+	ND	ND	+	+*
Corpus Lut.	+	+	+	+	+	-	+	+	+
Wound	+	ND	+	ND	+/-	+/-	ND	+	+

\* hevin was localized to both endothelial cells and malignant cells in brain tissue.

ND: not determined.





		27	2	3	1	0	GTP-binding protein
28	CTCTCACCT	13	1	0	0	0	ESTs
29	TCGTGCTTIG	13	1	4	2	1	feline sarcoma viral (v-feb) - Fujinami avian sarcoma viral (v-fps) homolog
30	GAGCAGTGCT	10	1	0	1	0	ESTs
31	CTCTAAAAA	10	1	0	0	1	phospholipase C, beta 4
32	GAACCCCGGT	10	1	7	15	1	ESTs
33	AACACAGTGC	10	1	7	15	1	ESTs